

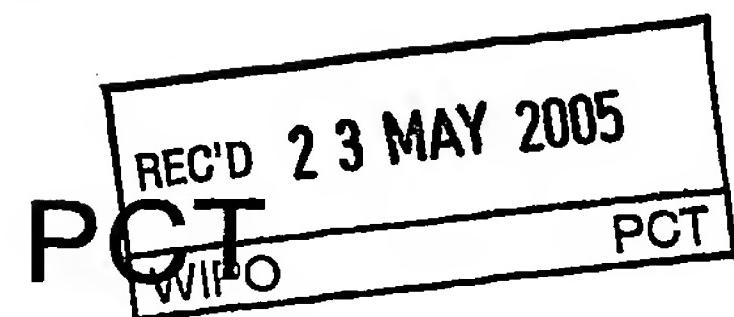
PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

E8/7

see form PCT/ISA/220



WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

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|--|--|--|---|
| <p>Applicant's or agent's file reference see form PCT/ISA/220</p> | | | <p>Date of mailing (day/month/year) see form PCT/ISA/210 (second sheet)</p> |
| <p>International application No. PCT/GB2005/000071</p> | <p>International filing date (day/month/year) 11.01.2005</p> | <p>Priority date (day/month/year) 14.01.2004</p> | |
| <p>International Patent Classification (IPC) or both national classification and IPC C07D211/46, A61K31/445, A61P3/00, A61P35/00</p> | | | |
| <p>Applicant CELLTECH R&D LIMITED</p> | | | |

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1b/s(b) that written opinions of this International Searching Authority will not be so considered.

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For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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|---|---|
| <p>Name and mailing address of the ISA:</p> <p> European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465</p> | <p>Authorized Officer</p> <p>Stix-Malaun, E Telephone No. +49 89 2399-8057</p> |
|---|---|



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000071

Box No. I Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
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 - a. type of material:
 a sequence listing
 table(s) related to the sequence listing
 - b. format of material:
 in written format
 in computer readable form
 - c. time of filing/furnishing:
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4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000071

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application,
- claims Nos. 1-30 (part)

because:

- the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (specify):
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the whole application or for said claims Nos. 1-30 (part)
- the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

- has not been furnished
- does not comply with the standard

the computer readable form

- has not been furnished
- does not comply with the standard

- the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

- See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000071

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N) Yes: Claims
 No: Claims 1-30

Inventive step (IS) Yes: Claims
 No: Claims 1-30

Industrial applicability (IA) Yes: Claims 1-30
 No: Claims

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.
PCT/GB2005/000071

III NON-ESTABLISHMENT

Present claims 1-30 (part) relate to compounds defined by reference to a desirable characteristic or property, namely "prodrug" and "protecting group". The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to compounds as defined in the formulae (I) and (III) and esters thereof and benzyl protected derivatives thereof.

V REASONED STATEMENT

1. PRIOR ART

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- D1: EP-A-0 536 402 (NIPPON SHINYAKU COMPANY, LIMITED) 14 April 1993 (1993-04-14)
- D2: WO 99/24401 A (G.D. SEARLE & CO; JACOB, GARY, S) 20 May 1999 (1999-05-20)
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have been considered for the examination procedure.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/GB2005/000071

2. NOVELTY

The subject-matter of the Claims is anticipated by D 1 and D2 (Article 33(2) PCT) (see for passages in the ISR).

The generic expressions (see for claims) form overlapping parts with present claims 1 and 30. Novelty cannot be established by merely disclaiming the exemplified compounds covered falling within said overlapping part. The whole overlapping range has to be removed.

In addition it is not clear for the assessment of novelty whether the additional substituents such as F, Cl..etc are actually to be interpreted "additional" (see for compound in the proviso containing methoxy as substituent).

3. INVENTIVE STEP

The subject-matter of the Claim does not fulfil the requirements of Article 33(3) PCT for the following reasons:

In the absence of a novel distinguishing feature inventive step cannot be assessed.

It is to be stated in a general manner that the compounds of D3 appear to solve the same problem. However they are structurally very close (see for passages in the ISR).

Accordingly the demonstration of unexpected beneficial effects vis à vis those compounds might be necessary.

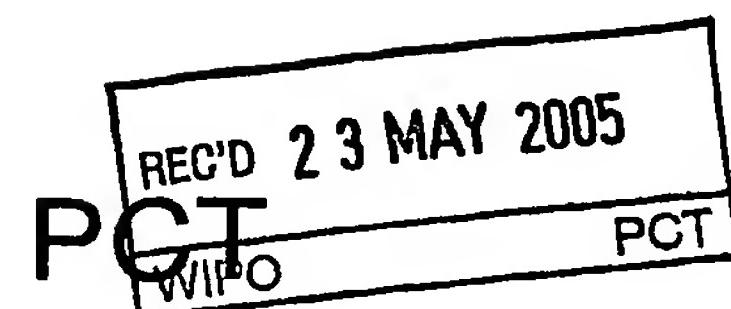
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Name and mailing address of the ISA:



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Authorized Officer

Stix-Malaun, E

Telephone No. +49 89 2399-8057



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000071

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
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2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. **type of material:**
 a sequence listing
 table(s) related to the sequence listing
 - b. **format of material:**
 in written format
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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000071

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application,
 claims Nos. 1-30 (part)

because:

- the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
 the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
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 the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

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 does not comply with the standard

the computer readable form

- has not been furnished
 does not comply with the standard

- the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

- See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000071

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N) Yes: Claims
 No: Claims 1-30

Inventive step (IS) Yes: Claims
 No: Claims 1-30

Industrial applicability (IA) Yes: Claims 1-30
 No: Claims

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/GB2005/000071

III NON-ESTABLISHMENT

Present claims 1-30 (part) relate to compounds defined by reference to a desirable characteristic or property, namely "prodrug" and "protecting group". The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to compounds as defined in the formulae (I) and (III) and esters thereof and benzyl protected derivatives thereof.

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International application No.
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2. NOVELTY

The subject-matter of the Claims is anticipated by D 1 and D2 (Article 33(2) PCT) (see for passages in the ISR).

The generic expressions (see for claims) form overlapping parts with present claims 1 and 30. Novelty cannot be established by merely disclaiming the exemplified compounds covered falling within said overlapping part. The whole overlapping range has to be removed.

In addition it is not clear for the assessment of novelty whether the additional substituents such as F, Cl..etc are actually to be interpreted "additional" (see for compound in the proviso containing methoxy as substituent).

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The subject-matter of the Claim does not fulfil the requirements of Article 33(3) PCT for the following reasons:

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PATENT COOPERATION TREATY

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REC'D 23 MAY 2005
PCT
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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

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| <p>Applicant's or agent's file reference see form PCT/ISA/220</p> | | <p>FOR FURTHER ACTION See paragraph 2 below</p> |
| <p>International application No. PCT/GB2005/000071</p> | <p>International filing date (day/month/year) 11.01.2005</p> | <p>Priority date (day/month/year) 14.01.2004</p> |
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Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Stix-Malaun, E

Telephone No. +49 89 2399-8057



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000071

Box No. I Basis of the opinion

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000071

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|-------------------------------|------|--------|------|
| Novelty (N) | Yes: | Claims | |
| | No: | Claims | 1-30 |
| Inventive step (IS) | Yes: | Claims | |
| | No: | Claims | 1-30 |
| Industrial applicability (IA) | Yes: | Claims | 1-30 |
| | No: | Claims | |

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
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International application No.
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